Page 78, lines 17-28, delete current paragraph and insert therefor:

Example 13: Detection of viral antigens in the lymphocyte cultures.

a15

The presence of specific retroviral antigens was investigated using the two pools of antibodies directed against MSRV-1 proteins. The results of immunofluorescence on the cultures inoculated with LES or GRE ultracentrifuged CS, obtained with the two pools (pool 2 = mouse monoclonals, pool 1 = rabbit polyclonals), are shown in Table 6 for donors 10 and 11. The numbers represent the percentages of cells exhibiting fluorescence intensities included between channels 100 and 1000.

IN THE CLAIMS:

Please cancel claims 72 and 75-77 without prejudice to or disclaimer of the subject matter contained therein.

Please replace claims 4-14, 18-25, 28, 31, 33-47, 50-57, 60-68, 70, 71, 73 and 74 as follows:

a16

4. (Amended) The method as claimed ~~in~~ claim 2, characterized in that a majority expansion of lymphocytes bearing a Vβ16 determinant and a co-expansion of lymphocytes bearing Vβs chosen from at least any one of Vβ2, Vβ3, Vβ7, Vβ8, Vβ12, Vβ14, Vβ17 and Vβ22 are demonstrated.

5. (Amended) The method as claimed in claim 3, characterized in that a majority loss of lymphocytes bearing a Vβ16 determinant and a co-decrease of lymphocytes bearing Vβs chosen from at least any one of Vβ2, Vβ3, Vβ7, Vβ8, Vβ12, Vβ14, Vβ17 and Vβ22 are demonstrated.

6. (Amended) The method as claimed in claim 1, characterized in that the biological sample originates from a patient suffering from an autoimmune disease.

7. (Amended) The method for detecting superantigen activity as claimed in claim 1, characterized in that:

(i) a culture supernatant of blood mononucleated cells or of choroid plexus cells or of leptomeningeal cells, said cells originating from patients suffering from an autoimmune disease or suspected of having a risk of developing the disease or of an established cell line, is sampled, and

(ii) said culture supernatant, or a part of the culture supernatant is brought into contact with a series of cultures of blood mononucleated cells originating from healthy donors, and

(iii) said expansion and, optionally, a co-expansion, or said loss and, optionally, co-decrease, of the blood mononucleated cells of step (ii) are detected.

8. (Amended) The method as claimed in claim 7, characterized in that the blood mononucleated cells originating from patients originate from patients suffering from multiple sclerosis (MS) and are chosen from monocytes and B lymphocytes and the blood mononucleated cells originating from healthy donors are chosen from T lymphocytes.

9. (Amended) The method for detecting superantigen activity as claimed in claim 1, characterized in that:

(i) blood mononucleated cells are sampled, said cells originating from patients suffering from an autoimmune disease or from patients suspected of having a risk of developing an autoimmune disease, and from healthy individuals,

(ii) said blood mononucleated cells originating from patients or from healthy individuals are brought into contact with culture supernatants, or a fraction of culture supernatant, of cells chosen from blood mononucleated cells, choroid plexus cells and leptomeningeal cells, and cells derived from established cell lines, and

(iii) said expansion and, optionally, co-expansion, or said loss and, optionally, co-decrease, using the blood mononucleated cells of step (i) are detected.

Cont Q16

10. (Amended) The method as claimed in claim 7, characterized in that said expansion and, optionally, co-expansion is demonstrated using ligands, each ligand being specific for a determinant chosen from Vβ16, Vβ2, Vβ3, Vβ7, Vβ8, Vβ12, Vβ14, Vβ17 and Vβ22, and in that said loss and, optionally co-decrease is demonstrated using ligands, each ligand being specific for a determinant chosen from Vβ16, Vβ2, Vβ3, Vβ7, Vβ8, Vβ12, Vβ14, Vβ17 and Vβ22.

11. (Amended) The method as claimed in claim 10, characterized in that the ligand is an antibody.

12. (Amended) The method as claimed in claim 7, characterized in that in order to demonstrate said expansion and, optionally, co-expansion or said loss and, optionally, co-decrease, the following is carried out

(i) extraction of the total RNAs from the blood mononucleated cells which have been placed together with MS culture supernatant or a fraction of MS culture supernatant and together with control culture supernatant or a fraction of control culture supernatant,

(ii) reverse transcription of said RNAs,

(iii) amplification specific for each Vβ family using a given pair of primers,

(iv) labeling of the amplification products obtained, with any suitable label,

(v) electrophoresis of said amplification products and analysis of the electrophoretic profiles obtained, using a suitable detector.

13. (Amended) The method as claimed in claim 12, characterized in that the blood mononucleated cells originating from patients originate from patients suffering from MS and are chosen from lymphocytes.

14. (Amended) A method for detecting a pathological condition or a predisposition to a pathological condition, in a biological sample, characterized in that at least one of the following parameters is demonstrated:

superantigen activity, characterized in that a majority expansion of lymphocytes bearing a Vβ16 and/or Vβ17 determinant or a majority loss of lymphocytes bearing a Vβ16 and/or Vβ17 determinant is demonstrated,

stimulation of the production of cytokines, and

induction of cellular apoptosis.

18. (Amended) The method as claimed in claim 7, characterized in that the pathological condition is associated with an autoimmune disease.

19. (Amended) The method as claimed in claim 1, characterized in that the superantigen activity is induced directly or indirectly by an effector agent chosen from proteins and/or microorganisms and/or pathogenic agents.

20. (Amended) The method as claimed in claim 19, characterized in that the microorganism is chosen from bacteria and retroviruses.

21. (Amended) The method as claimed in claim 19, characterized in that the superantigen activity is induced by the envelope protein of MSRV-1 referenced in SEQ ID No. 2 or by a fragment of said protein.

22. (Amended) The method as claimed in claim 19, characterized in that the superantigen activity is induced by the *env* gene of MSRV-1 referenced in SEQ ID No. 1 or a fragment of said gene.

23. (Amended) A human retrovirus, which has superantigen activity and is associated with an autoimmune disease, characterized in that the retrovirus is MSRV-1 and in that the superantigen activity is induced by the expression of the *env* gene of MSRV-1 or of a fragment of said gene.

24. (Amended) A human retrovirus, which has superantigen activity and is associated with an autoimmune disease, characterized in that the retrovirus is MSRV-1 and in

that the superantigen activity is induced by the env protein of MSRV-1 or by a fragment of said protein.

25. (Amended) A nucleic acid molecule comprising at least one or more fragment(s) of the RNA or of the DNA of the *env* gene of MSRV-1, identified by SEQ ID No. 1, said fragment being at least 18 nucleotides in length.

28. (Amended) A polypeptide molecule comprising at least one or more fragment(s) of the env protein of MSRV-1 identified by SEQ ID No. 2, said fragment being at least 6 amino acids in length.

31. (Amended) A vector comprising nucleic acid molecules as defined in claim 25.

33. (Amended) The method as claimed in claim 32, characterized in that:

(i) a culture supernatant of blood mononucleated cells or of choroid plexus cells or of leptomeningeal cells, said cells originating from patients suffering from an autoimmune disease or suspected of having a risk of developing the disease or of an established cell line, is sampled, and

(ii) said culture supernatant, or a part of the culture supernatant is brought into contact with a series of cultures of blood mononucleated cells originating from healthy donors, and

(iii) said expansion and, optionally, a co-expansion, or said loss and, optionally, co-decrease, of the blood mononucleated cells of step (ii) are detected.

34. (Amended) The method as claimed in claim 33, characterized in that the blood mononucleated cells originating from patients originate from patients suffering from MS and are chosen from B lymphocytes and monocytes and the blood mononucleated cells originating from healthy donors are chosen from T lymphocytes.

Cxt Q20

35. (Amended) The method as claimed in claim 32, characterized in that:

(i) blood mononucleated cells are sampled, said cells originating from patients suffering from an autoimmune disease or from patients suspected of having a risk of developing an autoimmune disease, and from healthy individuals,

(ii) said blood mononucleated cells originating from patients or from healthy individuals are brought into contact with culture supernatants, or a fraction of culture supernatant, of cells chosen from blood mononucleated cells, choroid plexus cells and leptomeningeal cells, and cells derived from established cell lines, and

(iii) said expansion and, optionally, co-expansion, or said loss and, optionally, co-decrease, using the blood mononucleated cells of step (i) are detected.

36. (Amended) The method as claimed in claim 32, characterized in that:

(i) a culture supernatant of blood mononucleated cells or of choroid plexus cells or of leptomeningeal cells, said cells originating from patients suffering from an autoimmune disease or suspected of having a risk of developing the disease or of an established cell line, is sampled, and

(ii) said culture supernatant, or a part of the culture supernatant is brought into contact with a series of cultures of blood mononucleated cells originating from healthy donors, and

(iii) said expansion and, optionally, a co-expansion, or said loss and, optionally, co-decrease, of the blood mononucleated cells of step (ii) are detected using a ligand or amplification combined with electrophoresis.

37. (Amended) The method for detecting superantigen activity as claimed in claim 1, characterized in that

(i) a polypeptide as identified by SEQ ID No. 2, or a fragment of said polypeptide, is produced or synthesized,

(ii) said polypeptide is brought into contact with a series of cultures of blood mononucleated cells originating from healthy donors, and

(iii) said expansion and, optionally, a co-expansion, or said loss and, optionally, co-decrease, of the blood mononucleated cells of step (ii) are detected.

38. (Amended) The method for detecting superantigen activity as claimed in claim 1, characterized in that:

(i) blood mononucleated cells are sampled, said cells originating from patients suffering from an autoimmune disease or from patients suspected of having a risk of developing an autoimmune disease, and from healthy individuals,

(ii) said blood mononucleated cells originating from patients or from healthy individuals are brought into contact with a polypeptide or a recombinant protein, as identified in SEQ ID No. 2, or a fragment of said polypeptide, and

(iii) said expansion and, optionally, co-expansion, or said loss and, optionally, co-decrease, using the blood mononucleated cells of step (i) are detected.

39. (Amended) The method as claimed in claim 38, characterized in that a polypeptide comprising at least one or more fragment(s) of the env protein of MSRV-1 identified by SEQ ID No. 2, said fragment being at least 6 amino acids in length, is used.

40. (Amended) The method as claimed in claim 37, characterized in that said polypeptide is encoded by a nucleic acid comprising at least one or more fragment(s) of the RNA or of the DNA of the *env* gene of MSRV-1, identified by SEQ ID No. 1, said fragment being at least 18 nucleotides in length, or a vector comprising said nucleic acid.

41. (Amended) A method for evaluating the effectiveness of an agent or of a composition in inhibiting superantigen activity in a biological sample, characterized in that

Cont
Q20

(i) a culture supernatant of blood mononucleated cells, or of choroid plexus cells or of leptomeningeal cells, said cells originating from patients suffering from an autoimmune disease or of cells of an established cell line, is sampled,

(ii) said supernatant, or a part of the culture supernatant, is brought into contact with a series of cultures of blood mononucleated cells originating from healthy donors, in the presence of said agent or of said composition at predetermined doses, and

(iii) the inhibition of said expansion and, optionally, co-expansion, or the inhibition of said loss and, optionally, co-decrease, of the lymphocytes bearing at least one determinant chosen from Vβ16, Vβ2, Vβ3, Vβ7, Vβ8, Vβ12, Vβ14, Vβ17 and Vβ22 are detected using a ligand specific for said determinant or amplification specific for each Vβ family using a given pair of primers combined with electrophoresis of said amplification products.

42. (Amended) A method for evaluating the effectiveness of an agent or of a composition in inhibiting superantigen activity in a biological sample, characterized in that

(i) a polypeptide is produced or synthesized,

(ii) said polypeptide is brought into contact with a series of cultures of blood mononucleated cells originating from healthy donors, in the presence of said agent or of said composition at predetermined doses, and

(iii) the inhibition of said expansion and, optionally, co-expansion, or the inhibition of said loss and, optionally, co-decrease, of the lymphocytes bearing at least one determinant chosen from Vβ16, Vβ2, Vβ3, Vβ7, Vβ8, Vβ12, Vβ14, Vβ17 and Vβ22 are detected using a ligand specific for said determinant or amplification specific for each Vβ family using a given pair of primers combined with electrophoresis of said amplification products.

43. (Amended) A method for evaluating the effectiveness of an agent or of a composition in inhibiting superantigen activity in a biological sample, characterized in that

(i) blood mononucleated cells are sampled, said cells originating from patients suffering from an autoimmune disease or suspected of having a risk of developing the disease, and from healthy individuals,

(ii) said blood mononucleated cells originating from patients or from healthy individuals are brought into contact with culture supernatants, or a fraction of culture supernatant, of cells chosen from blood mononucleated cells, choroid plexus cells, leptomeningeal cells and cells derived from established cell lines, and

(iii) the inhibition of said expansion and, optionally, co-expansion, or the inhibition of said loss and, optionally, co-decrease, of the lymphocytes bearing at least one determinant chosen from Vβ16, Vβ2, Vβ3, Vβ7, Vβ8, Vβ12, Vβ14, Vβ17 and Vβ22 using the blood mononucleated cells of step (i), in the presence of said agent or of said composition at given doses, are detected using a ligand specific for said determinant or amplification specific for each Vβ family using a given pair of primers combined with electrophoresis of said amplification products.

44. (Amended) A method for evaluating the effectiveness of an agent or of a composition in inhibiting superantigen activity in a biological sample, characterized in that

(i) blood mononucleated cells are sampled, said cells originating from patients suffering from an autoimmune disease or suspected of having a risk of developing the disease and from healthy individuals,

(ii) said blood mononucleated cells originating from patients or from healthy individuals are brought into contact with a polypeptide or a recombinant protein, and

(iii) the inhibition of said expansion and, optionally, co-expansion, or the inhibition of said loss and, optionally, co-decrease, of the lymphocytes bearing at least one

determinant chosen from Vβ16, Vβ2, Vβ3, Vβ7, Vβ8, Vβ12, Vβ14, Vβ17 and Vβ22 using the blood mononucleated cells of step (i), in the presence of said agent or of said composition at given doses, are detected using a ligand specific for said determinant or amplification specific for each Vβ family using a given pair of primers combined with electrophoresis of said amplification products.

45. (Amended) The method as claimed in claim 41, characterized in that the cells originate from a patient suffering from an autoimmune disease.

46. (Amended) The method as claimed in claim 41, characterized in that the blood mononucleated cells originate from patients suffering from MS and are chosen from B lymphocytes and monocytes.

47. (Amended) A method for evaluating the prophylactic and/or therapeutic effectiveness of an agent or of a composition with respect to a pathological condition and/or to a predisposition to a pathological condition, characterized in that inhibition of superantigen activity in a biological sample is demonstrated as described in claim 41.

50. (Amended) The method as claimed in claim 48, characterized in that the cells originate from a patient suffering from an autoimmune disease.

51. (Amended) The method as claimed in claim 48, characterized in that the blood mononucleated cells originate from patients suffering from MS and are chosen from B lymphocytes and monocytes.

52. (Amended) A method for evaluating the prophylactic and/or therapeutic effectiveness of an agent or of a composition with respect to a pathological condition and/or to a predisposition to a pathological condition, characterized in that inhibition of superantigen activity in a biological sample is demonstrated as described in claim 48.

53. (Amended) Composition for therapeutic and/or prophylactic use, characterized in that it comprises, inter alia, a therapeutic agent capable of inhibiting superantigen activity in a

biological sample, said superantigen activity being characterized in that a majority expansion of lymphocytes bearing a Vβ16 and/or Vβ17 determinant or a majority loss of lymphocytes bearing a Vβ16 and/or Vβ17 determinant is demonstrated, optionally in combination with a pharmaceutically acceptable excipient and/or adjuvant and/or diluent.

54. (Amended) The composition as claimed in claim 53, characterized in that the therapeutic agent is an antiviral agent.

55. (Amended) Composition as claimed in claim 53, characterized in that the therapeutic agent is chosen from a natural molecule and/or a recombinant molecule, or a fragment of said molecules, the protein sequence of which corresponds to the sequence of the Vβ16 and/or Vβ17 molecules, optionally in combination with one or more natural and/or recombinant molecules, or a fragment of said molecules, the protein sequence of which corresponds to the sequence of the Vβ2, Vβ3, Vβ7, Vβ8, Vβ12, Vβ14, Vβ17 and Vβ22 molecules.

56. (Amended) Composition as claimed in claim 53, characterized in that the therapeutic agent is chosen from a natural molecule and/or a recombinant molecule, or a fragment of said molecules, the protein sequence of which corresponds to the sequence of the Vβ16 and/or Vβ17 molecules, and optionally in combination with one or more natural and/or recombinant molecules or a fragment of said molecules, the protein sequence of which corresponds to the Vβ7, Vβ14 and Vβ17 molecules.

57. (Amended) The composition as claimed in claim 53, characterized in that the therapeutic agent is chosen from the natural and/or recombinant and/or synthetic molecules, or a fragment of said molecules.

60. (Amended) The prophylactic and/or therapeutic composition as claimed in claim 53, characterized in that the prophylactic and/or therapeutic agent is chosen from at least one ligand capable of interacting with Vβ16 and/or Vβ17, optionally in combination with at

least one ligand capable of interacting with at least one of Vβ2, Vβ3, Vβ7, Vβ8, Vβ12, Vβ14, Vβ17 and Vβ22.

61. (Amended) The composition as claimed in claim 60, characterized in that the ligand is capable of interacting with a retrovirus, its proteins and/or its nucleic acids.

62. (Amended) The composition as claimed in claim 60, characterized in that the ligand is an antiviral agent.

63. (Amended) The composition as claimed in claim 60, characterized in that the ligand is chosen from antibodies.

64. (Amended) The composition as claimed in claim 61, characterized in that the ligand is chosen from anti-MSRV-1 antibodies.

65. (Amended) The prophylactic and/or therapeutic composition as claimed in claim 53, characterized in that the prophylactic and/or therapeutic agent is chosen from at least one ligand capable of interacting with Vβ16 and/or Vβ17, optionally in combination with at least one ligand capable of interacting with at least one of Vβ7, Vβ14, Vβ17 and Vβ22.

66. (Amended) The composition as claimed in claim 60, characterized in that the ligand is capable of interacting with a retrovirus, its proteins and/or its nucleic acids.

67. (Amended) The composition as claimed in claim 63, characterized in that the ligand is chosen from antibodies.

68. (Amended) The composition as claimed in claim 63, characterized in that the ligand is chosen from anti-MSRV-1 antibodies.

70. (Amended) A therapeutic and/or prophylactic composition, characterized in that the therapeutic and/or prophylactic agent is chosen from at least one cell genetically modified *in vitro* with a therapeutic agent which consists of at least one nucleic acid molecule encoding at least one molecule, the protein sequence of which has a superantigen activity characterized in

that a majority expansion of lymphocytes bearing a Vβ16 and/or Vβ17 determinant or a majority loss of lymphocytes bearing a Vβ16 and/or Vβ17 determinant is demonstrated.

71. (Amended) The composition as claimed in claim 53, characterized in that the therapeutic and/or prophylactic agent is chosen from at least one cell genetically modified *in vitro* with a therapeutic agent which consists of at least one nucleic acid molecule encoding at least one ligand capable of interacting with Vβ16 and/or Vβ17.

73. (Amended) A method for identifying substances capable of blocking the transcription and/or the translation of a human retrovirus, according to which,

the substance is brought into contact with cells expressing a retroviral polypeptide, which has superantigen activity, said polypeptide comprising at least one or more fragment(s) of the env protein of MSRV-1 identified by SEQ ID No. 2, said fragment being at least 6 amino acids in length, and

a loss or decrease of the superantigen activity is detected as described in claim 1.

74. (Amended) A kit for screening substances capable of blocking the superantigen activity of a retrovirus associated with an autoimmune disease, or capable of blocking the transcription and/or the translation of said retrovirus, comprising:

cells expressing, at their surface, class II MHC products, transformed with and functionally expressing a retroviral superantigen,

cells bearing receptor chains having one or more Vβs stimulated by the retroviral superantigen, and

means for detecting a loss or decrease of the superantigen activity as described in claim 1.

REMARKS

Claims 1-71, 73 and 74 are pending. Claims 4-14, 18-25, 28, 31, 33-47, 50-57, 60-68, 70, 71, 73 and 74 are amended and claims 72 and 75-77 are cancelled herein.